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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,484	02/05/2001	John H. Griffin	SCRIP1200-1	8867

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/777,484	GRIFFIN ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-2, 4-5, 7, 9-10, 12-13, 15-16, 19, and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4, 7, 9-10, 12, 15, 16, and 22* is/are rejected.

7)☒ Claim(s) *5,13 and 19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 15 April 2005 under 37 CFR 1.114 based on parent Application No. 09/777,484 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 15 April 2005 has been entered in full. Claims 5, 9, 13, 15, 19 are amended. Claims 3, 6, 8, 11, 14, 17-18, and 20-21 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-2, 4-5, 7, 9-10, 12-13, 15-16, 19, and 22 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejection to claims 15-16, 19, and 22 under 35 U.S.C. 112, second paragraph, as set forth at pg 2 of the previous Office Action (14 October 2004) is *withdrawn* in view of amended claim 15 (15 April 2005).

2. The rejections of claims 1-2, 4-5, 7, 9-10, 12-13, 15, 19, and 22 under 35 U.S.C. § 103(a) as set forth at pg 4-8 of the previous Office Action (14 October 2004) are *withdrawn in part* in view of amended claims 5, 13, and 19, which now recite dosage limitations of Protein S. Please see 35 U.S.C. 103(a), below.

Claim Objections

3. Claims 5, 13, and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 102

4. Claims 1-2, 4, 9-10, 12, 15, and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Grinnell et al. (U.S. Patent 6,268,337). The basis for this rejection is set forth for the claims at pg 3-4 of the previous Office Action of 14 October 2004 and at pg 3-4 of the Office Action of 03 May 2004.

Applicant's arguments (15 April 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant states that the claims at issue do not recite open-ended language that does not exclude additional, unrecited elements or methods steps. Applicant submits that although claim 1 may include additional, unrecited elements, the limitation "...a therapeutically effective amount of activated protein C (APC) in a bolus injection," refers to a bolus injection containing the entire amount of APC that will ameliorate the cause or symptoms of the disease. Applicant asserts that Grinnell '337 teaches that "the APC will be administered by injecting a portion of the appropriate dose per hour as a bolus injection over time form about 5 minutes to about 120 minutes, followed by continuous infusion". Applicant contends that Grinnell is silent with regard to providing the entirety of the APC dose in a single bolus injection.
Applicant's arguments have been fully considered but are not found to be persuasive.
Specifically, Grinnell '337 teaches the administration of activated protein C (APC) to subjects

with vascular occlusive and arterial thromboembolytic disorders, including stroke (col 3-4; col 8, lines 28-33). Grinnell '337 discloses that APC may be administered intravenously or by injecting a portion of the appropriate dose per hour as a bolus injection (col 3-4, 7-8; col 4, lines 66-67). Although Applicant states that Grinnell '337 describes the use of bolus injection of APC in conjunction with continuous infusion of APC, claims 1-2, 4, 9-10, 12, 15, and 22 recite the term "comprising" which is open-ended language that does not exclude additional, unrecited elements or method steps (see MPEP § 2111.03). Furthermore, the instant claims only require a therapeutically effective amount of APC be administered in a bolus injection. Grinnell '337 meets this limitation because a therapeutically effective amount of APC is being administered to a subject in a bolus injection. Applicant is arguing limitations that are not present in the instant claims. The claims must independently define the invention for which patent protection is sought. Applicant is also reminded that a compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971)).

Claim Rejections - 35 USC § 103

5. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grinnell et al. (U.S. Patent 6,268,337) as applied to claims 1-2, 4, 9-10, 12, 15, and 22 above, and further in view of Hickenbottom et al. (Semin Neurol. 18(4):485-492, 1998). The basis for this rejection is set forth for at pg 4-8 of the previous Office Action (14 October 2004) and at pg 4-6 of the Office Action of 03 May 2004.

Applicant's arguments (15 April 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that Hickenbottom does not cure the deficiencies of Grinnell '337 (discussed above). Applicant indicates that Hickenbottom teaches that NMDA receptor antagonists and calcium channel antagonists are neuroprotective agents that are administered to acute stroke patients. Applicant argues that Hickenbottom does not describe the use of APC as a neuroprotective agent. Applicant contends that Hickenbottom is silent with regard to concentrations of any neuroprotective agents. Applicant submits that it would not have been obvious, taking the disclosure of the art cited with regard to the effects of APC treatment on thromboembolism, in combination with Hickenbottom's discussion of possible neuroprotective agents for combating the negative effects of ischemia, to consider and then examine the possibility of using APC as a neuroprotective agent. Applicant states that there is no reason to combine the disclosures of Grinnell and Hickenbottom.

Applicant's arguments have been fully considered but are not found to be persuasive. Grinnell '337 teaches the bolus and intravenous administration of a therapeutically effective amount of APC to subjects with vascular occlusive and arterial thromboembolytic disorders, *including stroke* (col 3-4; col 7-8, lines 28-33, 66-67). Grinnell '337 teaches that the administration of APC is beneficial in preventing the local extension of the microvascular and macrovascular occluding arterial thrombus, thereby reducing the *neurological* deficit resulting from stroke (abstract; col 2, lines 37-44). Hickenbottom teaches that neuroprotection relies on the principle that delayed neuronal injury occurs after ischemia. Hickenbottom also teaches that

NMDA receptor antagonists and calcium channel antagonists are neuroprotective agents that are administered to acute stroke patients (abstract; pg 487, col 2 through pg 489).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the APC administration method as taught by Grinnell '337 by coadministering neuroprotective agents, such as an NMDA receptor antagonist or a calcium ion channel antagonist, as taught by Hickenbottom. The person of ordinary skill in the art would have been motivated to make that modification because neurons suffer irreversible damage after only a few minutes of complete cessation of blood flow (such a condition existing during cardiac arrest) (pg 485, first paragraph). The person of ordinary skill in the art reasonably would have expected success because previous studies indicated the antithrombotic effects of APC and the neuroprotective effects of acute stroke therapy agents, such as NMDA antagonists and calcium channel antagonists. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

6. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grinnell et al. (U.S. Patent 6,268,337) as applied to claims 1-2, 4, 9-10, 12, 15, and 22 above, and further in view of Grinnell et al. (U.S. Patent 6,071,514). The basis for this rejection is set forth at pg 9 of the previous Office Action (14 October 2004) and at pg 6-8 of the Office Action of 03 May 2004.

Applicant's arguments (15 April 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that the combined references of Grinnell '337 and Grinnell '514 do not teach all of the claimed limitations.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed above, Grinnell '337 teaches the bolus and intravenous administration of a therapeutically effective amount of APC to subjects with vascular occlusive and arterial thromboembolytic disorders, *including stroke* (col 3-4; col 7-8, lines 28-33, 66-67). Grinnell '337 teaches that the administration of APC is beneficial in preventing the local extension of the microvascular and macrovascular occluding arterial thrombus, thereby reducing the *neurological* deficit resulting from stroke (abstract; col 2, lines 37-44). Grinnell et al. '337 does not teach the administration of a therapeutically effective amount of one or more anticoagulant, anti-platelet or thrombolytic agent. However, Grinnell '514 teaches the intravenous administration of activated protein C (APC) to subjects with thrombotic disorders (including, but not limited to, stroke, venous thrombosis, myocardial infarction, unstable angina, etc.) (col 3, lines 34-67 through col 4). Grinnell '514 also discloses that APC may be administered alone or in combination with an antiplatelet agent (col 3, lines 34-52).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the APC administration method as taught by Grinnell '337 by coadministering an anti-platelet agent as taught by Grinnell et al. '514. The person of ordinary skill in the art would have been motivated to make that modification because blood coagulation is a complex process regulated by the balance of pro-coagulant and anticoagulant mechanisms, wherein this balance determines normal hemostasis or abnormal pathological thrombus formation. The person of ordinary skill in the art reasonably would have expected success

because previous studies indicated the antithrombotic effects of APC and the reduction of the tendency of platelets in the blood to clump and clot after administration of anti-platelet factors (like aspirin). Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
06 June 2005

Bridget E. Bunner
patent examiner